Low-Dose Short Course Tertiary Prophylaxis in Hemophilia A Patients with Target Joint

Bunchoo Pongtanakul, MD., Thaneeporn Intra, MD., Nattee Narkbunnam, MD.

Division of Hematology and Oncology, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Introduction

Full-dose prophylaxis is the recommended treatment for severe hemophilia A for maintain musculoskeletal health.[1] Unfortunately, full-dose prophylaxis is not affordable in Thailand due to the limitation of government budget. The previous study demonstrated the efficacy of low-dose tertiary prophylaxis to decrease bleeding rate.[2]

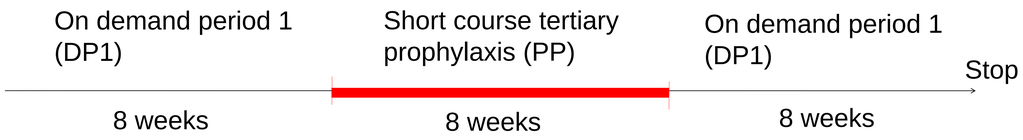
Objective

The aim of this study was to evaluate the efficacy of low-dose short course tertiary prophylaxis to reduce bleeding rate in hemophilia A patients with target joint compare to on demand treatment.

Methods

Moderate and severe hemophilia with target joint were eligible. This study consisted of 3 periods; on demand period 1 (DP1), prophylaxis period (PP) and on demand period 2 (DP2). Each period was 8 weeks long. During PP, patients received factor VIII concentrate 10 IU/kg 2 times per week. Bleeding rate, target joint circumference, range of motion, number of factor VIII concentrate use and complications were recorded for each period.

Figure1: Study design



- DP1: FVIII concentrate given on demand at the time of clinically evident bleeding
- PP: FVIII concentrate **10 IU kg^{-1} twice weekly**
- DP2: FVIII concentrate given on demand at the time of clinically evident bleeding

Results

Seven patients were enrolled (moderate hemophilia A 57.1% and severe hemophilia A 42.9 %) with a mean age of 17.2 years (range 4-22.2 years). Bleeding rate during PP was significantly lower than those DP1: 3.5 and 17.5 times per month (P = 0.043). Hemarthrosis in target joints (HTJ) were also significantly lower during PP than those during DP1: 5 and 31 episodes (P = 0.018). However, total and bleeding rate and HTJ during DP1 and DP2 were not statistical significance (P =0.66 and 1, respectively). Factor VIII concentrate used during DP1, PP and DP2 period were 159.9, 801 and 143.4 IU/kg/month, respectively. Target joint circumference and rage of motion were not change and there was no occurrence of factor VIII inhibitor and other complications during the study period.

Table 1: Number of target joint bleeding episodes

Patient NO.	On demand 1 (DP1	Prophylaxis (PP)	On demand 2 (DP2)
1	7	0	10
2	12	4	8
3	2	0	1
4	4	1	3
5	1	0	0
6	2	0	5
7	3	0	2
Sum	31	5	29
Mean± SD	4.4 ± 3.9	0.7 ± 1.5	4.1 ±3.7
Median	3 (1-12)	0 (0-4)	3 (0-10)

Conclusions

Low-dose short course tertiary prophylaxis effectively reduces bleeding rate in moderate and severe hemophilia A. However, bleeding rate increased to previously untreated rate after stop prophylaxis. This may reflect that 8-week prophylaxis is not long enough to improve target joint disease. Nevertheless, effectively reduce bleeding rate and lower cost compared to full-dose prophylaxis. Low-dose prophylaxis may be an alternative choice of treatment for hemophilia A in developing country with limited resources.

Acknowledgement: Dr. B. Pongtanakul and Dr. N.Narkbunnam are supported by Chalermphrakiat Grant , Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

References

1.Manco-Johnson MJ, Abshire TC, Shapiro AD, Riske B, Hacker MR, Kilcoyne R, et al. Prophylaxis versus Episodic Treatment to Prevent Joint Disease in Boys with Severe Hemophilia. N Engl J Med 2007; 357(6):535-44.

2.Wu R, Luke KH, Poon MC, Wu X, Zhang N, Zhao L, et al. Low dose secondary prophylaxis reduces joint bleeding in severe and moderate haemophilic children: a pilot study in China. Hemophilia 2011; 17(1):70-4.